REMARKS

The Rejections

1. Claims 21, 24 and 26-36 are rejected under 35 U.S.C. §112, first paragraph, for an alleged lack possession, as set forth at pages 2-4 of the Official Action dated February 13, 2004.

2. Claims 14, 15, 19 and 21-36 are rejected under U.S.C. §112, first paragraph, for an alleged lack of possession, as set forth at pages 4-9 of the Official Action dated February 13, 2004.

3. Claims 14, 15, 19, and 21-36 are rejected under 35 U.S.C. §112, first paragraph, for an alleged lack of enablement, as set forth at pages 9-17 of the Official Action dated February 13, 2004.

4. Claims 21, 24, and 26-36 are rejected under U.S.C. §112, second paragraph, for indefiniteness, as set forth at pages 17-18 of the Official Action dated February 13, 2004.

Response to the Rejections

1. Claims 21, 24 and 26-36 Are Not Unpatentable Under 35 U.S.C. §112, First Paragraph, For Lack of Possession.

The phrase "deletion of amino acids 297-329 in said variable loop" recited in Claims 21, 24, 26, 27, 30, and 34 is not new matter.

Applicants submit herewith an executed Rule 132 Declaration of Dr. Danuta Kozbor. Dr. Kozbor is currently an Associate Professor in the Department of Immunology at the Roswell Park Cancer Institute in Buffalo, New York. Dr. Kozbor's C.V. is found in Exhibit 1 attached to her Declaration. She received her doctorate in 1982 and following a postdoctoral appointment from 1982-1985, Dr. Kozbor has been an academic scientist for the past 19 years, i.e., since 1985. She has been active in the field of HIV research, as

demonstrated by the research projects she has completed and the scientific publications that she has authored. See paragraphs (1)-(2) and Exhibit 1, pages 4-12 of the Declaration. Dr. Kozbor is an inventor of the present application.

Dr. Kozbor has read and understood the contents of the present application. In addition, she appreciates that the present application was filed on May 29, 1998. Dr. Kozbor has also read and understood the pending claims of the present application as well as the Official Actions dated June 25, 2003 and February 13, 2004. See paragraphs (3)-(9) of the Declaration.

At paragraphs (10)-(14) of the Declaration, Dr. Kozbor reviews the history of the discovery of HIV and different strains were named. Significantly, Dr. Kozbor states that different isolates may have slightly different sequences. In paragraph (15), Dr. Kozbor states:

> There are small sequence differences between these strains, but these differences are not significant for practicing the invention described in the above-identified application. In the invention described in the above-identified application, the essence is inducing a CTL response against conserved region by deleting the V3 loop, immunodominant region. Therefore, there is no need to practice the examples specifying all varieties of HIV-1 strains' sequences nor one specified sequence which can easily vary. Rather, it is sufficient to say, for example, "Δ V3 loop" or "V3 loop deletion." Typical sequences for HIV-1 IIIb such as HXB2 or BH10 had been available and well-recognized in the field of the invention at the time of filing date of the above-identified application.

In addition, at paragraph (16) of the Declaration, Dr. Kozbor explains the meaning of the symbol "Δ" used in the specification of the present application as follows:

> The notation "Δ" means the deletion or destruction of the indicated component. Thus, that notation was also well-known, common technical language among scientists in the field of the invention at the time the present application was filed. Thus, it would have been clear to those skilled in the field of the invention at the time the present application was filed that the expression "Δ V3 loop" means that the V3 loop was deleted.

At paragraphs (17)-(27) of the Declaration, Dr. Kozbor explains the history and relationship between the variable region V3 and the V3 loop. In paragraph (18) Dr. Kozbor states:

> Modrow et al. named conserved regions C1 to C6, and variable regions V1 to V5 (see FIG 2). In the figure shown in that reference, variable region V3 is from amino acid positions 300 to 321 in the BH10 isolate according to Table 2 or is from amino acid positions 300 to 329 in the BH10 isolate according to Fig. 1. After the publication of Modrow et al., the term "variable region 3 (V3)" became common language in the area of HIV research. The number, 300 or 321/329, may slightly vary strain by strain (report by report) because of virus mutability or a deficiency in the numbering standard for such variation. See Korber et al. 1998 (*HIV Molecular Immunology Compendium* 1998, Review articles, "Numbering Positions in HIV Relative to HXB2CG"), a copy of which is attached hereto as Exhibit 6. This difference was also recognized by those skilled in the field of the invention at the time the above-identified application was filed.

In paragraphs (19) and (20) of the Declaration, Dr. Kozbor discusses the 1990 paper from Leonard et al. (a copy of which is Exhibit 7 of the Declaration). Dr. Kozbor states:

> Leonard et al. showed conformational model indicating variable regions Vl to V5 in Figure 7, and variable region V3 is indicated on the loop formed by two cystein residues. This loop formation, protruding from the envelope protein surface, was quite understandable to those skilled in the field of the invention at the time the above-identified application was filed, since these variable regions are dominant epitopes. [Paragraph (19) of the Declaration, last two sentences.]

> In Figure 6, variable region V3 is indicated from amino acid positions 270 to 298, those omitting 30 amino acids of signal peptide, therefore, adjusting to BH-10 isolate sequence, this is equivalent to amino acid positions 300 to 328 in BH10 isolate (see sequential analysis sheet). Variable region V3 is located within the loop formed by two cystein residues at the amino acid positions 296 and 301 in the BH10 isolate. [Paragraph (20) of the Declaration.]

In paragraphs (21) and (22) of the Declaration Dr. Kozbor goes on to explain that

> As noted above, cystein residues forming the V3 loop do not vary among the strains having different sequences; therefore, the skilled person in the field of the invention can easily recognize the V3 loop, which is formed by two cystein residues located at 296 and 331 in HIV-1 IIIb variants. Even when this amino acid position numbering differs because of strain differences, one skilled in the field of the invention at the time the above-identified application was filed could have found the V3 loop by finding the corresponding two cystein residues or by finding the variable region V3 using a homology comparison.
>
> This is why the indicated position for "V3" which means "variable region V3" sometimes does not match the exact position for "V3 loop," such as described in Back et al. (*Journal of Virology*, Nov. 1993, pp. 6897-6902), a copy of which is attached hereto as Exhibit 9. This loop formation, i.e., the V3 loop, became common terminology in the field of the invention. After that, researchers commonly refer to the V3 loop as almost the same meaning as for variable region V3. This structural knowledge was well-accepted in the field of the invention prior the filing date of the above-identified application.

In paragraph (23) of the Declaration, Dr. Kozbor explains that the expression "V3 deletion" means "that the natural sequence of the third variable loop was replaced with the sequence GAG," based on work by Wyatts. Dr. Kozbor states that:

> His publications [Wyatts] support the observation that those skilled in the field of the invention recognized that a V3 deletion mutant constructed by Wyatts (Dr. Sodoroski's research group) included a GAG in place of the deleted portion of the sequence. This terminology was widely known to those skilled in the field of the invention at the time the present application was filed. [Paragraph (23) of the Declaration.]

Dr. Kozbor continues her analysis in paragraphs (24) and (25) stating:

> Even if the specification of the above-identified application does not refer to Wyatts but refers to a V3 deletion mutant, for example, those skilled in the field of the invention would have understood at the time the present application was filed what kind of construct was to be made, based on the knowledge described above. Even when just an indication to delete the V3 loop is given, the skilled person can understand

> which portion is to be deleted to obtain desired effect of the invention, and can find a suitable position to be deleted (note: 297-329 is apparently included in the V3 loop of IIIb variants such as BH10 or HXBc2). Also, to maintain the correct conformation of the envelope protein, the skilled person would understand closing the edge after deletion of V3 loop, and the easiest connecting peptides might be those consisting of small amino acid such as glycine or alanine.
>
> The V3 loop is located between two cystein residues located at amino acid positions 296 and 331 in HIV-1 IIIb variants. These cystein residues are not located around amino acid positions 99-110, which are the amino acid position calculated by, incorrectly, considering 297-329 as referring to the nucleotide position in the encoding nucleic acid, as suggested by the Examiner.

In paragraph (27) of the Declaration, Dr. Kozbor concludes:

> Based on the foregoing, the amino acid sequence of the envelope glycoprotein of HIV was well-known to those skilled in the field of the invention at the time the present application was filed in the U.S. In particular, the location of the variable region of the amino acid sequence was well-known to those skilled in the field of the invention. Thus, those skilled in the field of the invention at the time the present application was filed in the U.S would have appreciated that the description of the numbers 297 to 329 in the specification of the above-identified application was referring to the amino acid sequence of the protein and not to the nucleic acid sequence encoding that protein.

Applicants also submitted an executed Rule 132 Declaration of Dr. Alagarsamy Srinivasan with the Request for Reconsideration filed on November 25, 2003. Dr. Srinivasan has years of experience in the field of AIDS pathogenesis and vaccines. See paragraph (1) of the Declaration.

Dr. Srinivasan has read and understood the contents of the present application. In addition, she appreciates that the present application was filed on May 29, 1998. Dr. Srinivasan has also read and understood the pending claims of the present application as well as the Official Action dated June 25, 2003. See paragraphs (4)-(21) of the Declaration.

According to Dr. Srinivasan, the amino acid sequence of the envelope glycoprotein of HIV was well-known to those skilled in the field of the invention at the time the present application was filed in the U.S. In particular, the location of the hypervariable region of the amino acid sequence was well-known to those skilled in the field of the invention. In addition, it was well-known to those skilled in the field of the invention that the third variable loop (V3) of includes amino acids 297 to 329. Therefore, in Dr. Srinivasan's opinion, those skilled in the field of the invention at the time the present application was filed in the U.S would have appreciated that those numbers refer to the amino acid sequence of the protein, and do not refer to the nucleic acid sequence encoding that protein. According to Dr. Srinivasan, this is demonstrated by Back et al., *Journal of Virology*, Nov. 1993, pp. 6897-6902, a copy of which is attached to the Declaration as Exhibit 2. According to Dr. Srinivasan, Back et al. describe the gp41 coding region and the hypervariable region. See Figure 2 at page 6900 of Back et al., which explicitly describes that amino acids 297 to 329 are part of V3, i.e., the third variable loop. See paragraph (21) of the Declaration.

In Dr. Srinivasan's opinion, those skilled in the field of the invention at the time the present application was filed in the U.S would have appreciated that the vv-ΔV3 mutant with the Δ297-329 deletion prepared in Example 2 of the present application was a construct in which amino acids 297-329 of V3 were replaced with Gly-Ala-Gly. According to Dr. Srinivasan, this is demonstrated by the fact that Example 2 of the present application describes that the vv-ΔV3 mutant was constructed from ligation of fragments obtained by PCR amplification from the pSVIII-env plasmid, which was a gift from Dr. J. Sodroski (see page 26 of the present application). According to Dr. Srinivasan, the pSVIII-env plasmid is described in a scientific publication co-authored by Dr. Sodroski: Wyatt et al., Journal of Virology, Dec. 1992, pp. 6997-7004, a copy of which is attached to the Declaration as

Exhibit 3. The first paragraph of the Materials and Methods section of Wyatt et al. reads as follows:

> Mutant envelope glycoproteins. The HIV-1 (HXBc2 strain) envelope glycoprotein mutants used in this study were previously described (46). The Δ297-329 mutant contains a deletion spanning the V3 loop, with the sequence Gly-Ala-Gly inserted in place of the loop (62, 68). Envelope glycoproteins were expressed by transfection of ***plasmid pSVIII-env*** containing either a wild-type or mutated env gene into COS-1 cells by the DEAE-dextran technique (46). [Emphasis added.]

Thus, according to Dr. Srinivasan, Wyatt et al. explicitly states that the Δ297-329 mutant described in Example 2 of the present application had amino acid residues 297-329 replaced with Gly-Ala-Gly. Wyatt et al. also makes it apparent that the numbers "297-329" refer to amino acids in the protein sequence and not to base positions in the encoding nucleic acid sequence. See paragraph (22) of the Declaration.

Based on the foregoing, the phrase "deletion of amino acids 297-329 in said variable loop" recited in Claims 21, 24, 26, 27, 30, and 34 is not new matter. The Declarations of Dr. Kozbor and Dr. Srinivasan demonstrate that one would have appreciated that the specification was referring to the deletion of amino acids 297-329 in the third variable loop. Those Declarations provide explicit reasoning to support that conclusion. In addition, Dr. Kozbor's Declaration explicitly addresses the Examiner's comments at the top of page 4 of the Official Action dated February 13, 2004 regarding the amino acid numbers of the V3 loop. Accordingly, withdrawal of this ground of rejection is respectfully requested.

2. Claims 14, 15, 19 and 21-36 Are Not Unpatentable Under U.S.C. §112, First Paragraph, For Lack of Possession.

As the Examiner correctly notes, the claims specify a DNA encoding an envelope glycoprotein of HIV having a deletion of the third variable loop. At page 2, lines 13 to page 3, line 12 of the present specification, the V3 loop is discussed in detail, with citations to the

scientific literature. That discussion demonstrates that the existence of the V3 loop in HIV was well-known at the time the present application was filed. The specification also provides a discussion of deleting the V3 loop at page 22, line 20 to page 23, line 8.

The Examples of the present specification provide an explicit description of a nucleic acid encoding an envelope glycoprotein of HIV which comprises a deletion of the third variable loop. See, for example, Example 2 at pages 26-27 of the specification. In addition, the Dr. Kozbor's Declaration demonstrates that HIV sequences including the location of the V3 loop were known in art at the time the present application was filed.

In addition, according to Dr. Srinivasan, the generation of the 1ΔV3, 7ΔV3, and 8ΔV3 mutants has been described by Kmieciak et al., J. Immunol. 1998, 160:5676-5683 in the Materials and Methods section (a copy of Kmieciak et al. is attached to the Declaration as Exhibit 6). Dr. Srinivasan summarizes that method as follows. See paragraph (23) of the Declaration.

The HIV-1IIIB isolate was the source of the wild-type (WT) envelope (env) gene and the ΔV3 env mutant cloned in the pSC11-based vector under the control of a synthetic early/late vaccinia virus (vv) promoter. The 1ΔV3, 7ΔV3, and 8ΔV3 mutants are recombinant vv clones generated by homologous recombination of the pSC-ΔV3 plasmid using nonrecombinant vaccinia virus. They all express the Δ297-329 deletion of the env glycoprotein. See paragraph (23) of the Declaration.

The pSC-ΔV3 env plasmid was constructed by ligation of fragments obtained by PCR amplification from the pSVIII-env plasmid. One fragment was generated by PCR with the synthetic oligonucleotide containing the *Sal*I site and the CCACC Kozak's sequence in front of the ATG condon (5'-AGAGTCGACCCACCATGAGAGTGAAGGAGA-3', sense) and with the oligonucleotide (5'-ACAGGTACCCCATAATAGACTGTGAC-3', antisense) containing the *Kpn*I site. The second fragment was derived by *Kpn*I and *BamH*I digests of

the pSVIII-env plasmid, and the third fragment was generated by PCR with the synthetic oligonucleotide containing the *BamH*I site at its 5' end (5'-AACGGATCCTTAGCACTTATCTGGG-3', sense) and the antisense primer (5'-TTGCGCGGCCGCTTATAGCAAAATCCTTTCC-3') containing the TAA stop codon followed by the *Not*I site. The three fragments were ligated into the *Sal*I and *Not*I sites of the pSC-11-based vector to generate plasmid pSC-ΔV3. A similar approach was used to generate plasmid with the WT env gene (pSC-WTP) using the recombinant clone pIIIB. Plasmids pSC-ΔV3 and pSC-WTP were used to generate recombinant vv-ΔV3 (1ΔV3, 7ΔV3, 8ΔV3) and vv-WTP (WTP-2, WTP-5, and WTP-8) viruses by homologous recombination. Note, that only vv-WTP-2 and vv-7ΔV3 were used for functional studies including env-specific cytotoxic T cell responses and HIV gp120-mediated pathogenesis. See paragraph (23) of the Declaration.

As discussed above, it is Dr. Srinivasan's opinion that those skilled in the field of the invention at the time the present application was filed in the U.S would have appreciated that the vv-ΔV3 mutant with the Δ297-329 deletion prepared in Example 2 of the present application was a construct in which amino acids 297-329 of V3 were replaced with Gly-Ala-Gly.

In Dr. Srinivasan's opinion, the specification of the present application provides a detailed description of procedures for making the nucleic acid and cells recited in the Claims 14, 15, 19, and 21-36 of the present application and a description of how to use those cells for preparing a vaccine against HIV, for inducing cellular immunity against HIV, stimulating CTL activity against HIV, and stimulating a CTL response in a patient as specified in those claims. According to Dr. Srinivasan, one skilled in the field of the invention would have appreciated at the time the present application was filed in the U.S. that the inventors thereof were in possession of the invention as defined in the claims of the present application and that

those inventions could be practiced using routine experimentation. See paragraph (26) of the Declaration.

The Examiner states:

> The only DNA encoding an envelope glycoprotein of HIV having a deletion of the V3 loop described in the specification are vv-ΔV3 (pg 26, line 16), 1ΔV3, 7ΔV3, and 8ΔV3 (pg 34). [Official Action dated February 13, 2004 at page 4, paragraph (II).]

Thus, the Examiner agrees that the nucleic acid recited in the claims is described in the specification. To support the rejection, the Examiner argues:

> The specification does not provide adequate written description for one of skill ***to make*** vv-ΔV3 (pg 26, 16), 1ΔV3, 7ΔV3, and 8ΔV3; therefore, the specification does not provide adequate written description for DNA encoding an envelope glycoprotein of HIV having a deletion of the V3 loop as claimed. [Official Action dated February 13, 2004, sentence bridging pages 4-5; emphasis added.]

Thus, in arguing that the specification is deficient in describing how to make the recited nucleic acid, the Examiner is actually making a rejection based on lack of enablement and not a failure to satisfy the written description requirement.

In view of the foregoing, the present application satisfies the written description requirement. Accordingly, withdrawal of this ground of rejection is respectfully requested.

3. Claims 14, 15, 19 and 21-36 Are Not Unpatentable Under U.S.C. §112, First Paragraph, For Lack of Enablement.

At page 10 of the Official Action dated February 13, 2004, the Examiner stated that Applicants have not addressed the issue regarding the numbering of the amino acids recited in, for example, Claim 21. This issue was addressed in section (1) of this response relating to the new matter rejection.

Based on his review of the present application (see paragraphs (5)-(18) of the Declaration), it is Dr. Srinivasan's opinion that the specification of the present application provides a detailed description of procedures for making the nucleic acid and cells recited in the Claims 14, 15, 19, and 21-36 of the present application and a description of how to use those cells for preparing a vaccine against HIV, for inducing cellular immunity against HIV, stimulating CTL activity against HIV, and stimulating a CTL response in a patient as specified in those claims. See paragraph (26) of the Declaration.

In addition, according to Dr. Srinivasan, several articles were published after the present application was filed in the U.S. and demonstrate that the methods and procedures described in the present application described how to make and use compositions as specified in Claims 14, 15, 19, and 21-36 of the present application. Those publications are:

(a) Rowland-Jones et al., *Immunology Letters*, 1999, 00. 9-14 (a copy of which is attached to the Declaration as Exhibit 4);

(b) Kiszka et al., *Journal of Virology*, May 2002, pp. 4222-4232 (a copy of which is attached to the Declaration as Exhibit 5); and

(c) Kmieciak et al., *The Journal of Immunology*, 1998, pp. 5676-5683 (a copy of which is attached to the Declaration as Exhibit 6).

According to Dr. Srinivasan, Rowland-Jones et al. states that eliciting a CTL response is an important goal for developing a vaccine against HIV. See the Abstract and paragraph (28) of the Declaration.

Kiszka et al. is co-authored by the two inventors of the present application, i.e., Yutaro Kaneko and Danuta Kozbor. Kiszka et al. demonstrate the "vaccines expressing the ΔV3 mutant of either HIV -1IIIb or HIV-189.6 envelope glycoproteins induced broader CD8+ T-cell activities than those elicited by the wildtype (WT) counterparts." See the Abstract and paragraph (29) of the Declaration.

Kmieciak et al. is also co-authored by the two inventors of the present application. Kmieciak et al. describe that the ΔV3 mutant described in the present application increased CTL activities against conserved epitopes of the env glycoprotein. See the Abstract and paragraph (30) of the Declaration.

At page 8 of the Official Action dated February 13, 2004, the Examiner asserted:

> Applicants' conclusion [i.e., that the claims are enabled] is in error because it is not based on any scientific or logical reasoning or on the specification as originally filed. [First sentence of the last paragraph.]

That assertion is simply not correct. Applicants' conclusion is based to at least a large extent on the Declaration of Dr. Srinivasan. As discussed above, Dr. Srinivasan's opinions regarding the specification of the above-identified application are based on his careful review of that specification. In addition, Dr. Srinivasan discusses several publications from the scientific literature which demonstrate that the methods and procedures described in the present application described how to make and use compositions as specified in Claims 14, 15, 19, and 21-36 of the present application.

Clearly, Applicants' conclusion was based on scientific and logical reasoning as well as on the specification itself. It is not proper for the Examiner to simply ignore the opinions Dr. Srinivasan's Declaration in this manner.

In view of the foregoing, the claims are enabled. Withdrawal of this ground of rejection is respectfully requested.

4. Claims 21, 24 and 26-36 Are Not Unpatentable Under 35 U.S.C. §112, Second Paragraph.

As discussed above, it is Dr. Srinivasan's opinion that those skilled in the field of the invention at the time the present application was filed in the U.S would have appreciated that the vv-ΔV3 mutant with the Δ297-329 deletion prepared in Example 2 of the present

application was a construct in which amino acids 297-329 of V3 were replaced with Gly-Ala-Gly.

Claims 28-36 are not indefinite. In Claim 28, (a) simply specifies that a nucleic acid encoding an envelope protein of HIV which comprises a deletion of the third variable loop is introduced into a vector DNA or a liposome. The meaning of "introducing" is well-known to those skilled in the art. In addition, the term "vector" is described at the last two lines of page 9 of the specification. So, a DNA vector is simply such a vector composed of DNA. Even though putting a nucleic acid into a vector is different from putting a nucleic acid into a liposome, there is nothing indefinite about reciting those alternative embodiments in a single claim.

Regarding Claims 29 and 33, if the claims do not specify the identity of the adjuvant, then the adjuvant recited in Claim 29 may be the same or different from the adjuvant recited in Claim 28.

In addition, according to Dr. Srinivasan, the phrase "introducing into a vector DNA or liposome a nucleic acid encoding an envelope glycoprotein of HIV," as recited in Claim 28, would not have been unclear to those skilled in the art when the present application was filed in the U.S. That phrase simply means that a nucleic acid which encodes an envelope glycoprotein of HIV is introduced into a vector DNA or liposome. See paragraph (31) of the Declaration.

In Dr. Srinivasan's opinion, the meaning of the term "introducing" such a nucleic acid into a vector DNA or liposome, as recited in Claim 28, was well-known in the field of the invention at the time the present application was filed in the U.S. Moreover, the specification of the present application explains such a procedure in detail, and even provides specific Examples thereof. See paragraph (32) of the Declaration.

According to Dr. Srinivasan, the fact that Claim 28 recites vector DNA or liposome as alternatives would not have confused those skilled in the art when the present application was filed in the U.S., because there is nothing confusing about the meaning of two alternatives in the claim. See paragraph (33) of the Declaration.

In Dr. Srinivasan's opinion, the meaning of the term "vector DNA" as recited in Claim 28 would have been readily appreciated by those skilled in the field of the invention at the time the present application was filed in the U.S. That term is defined in the specification of the present application at page 9, lines 20-21. See paragraph (34) of the Declaration.

According to Dr. Srinivasan, the meaning of Claim 29 would have been readily appreciated by those skilled in the field of the invention at the time the present application was filed in the U.S. It would have been appreciated that the adjuvant recited in Claim 29 could be the same as or different from the adjuvant specified in Claim 28. See paragraph (35) of the Declaration.

Based on the foregoing, the claims are definite within the meaning of 35 U.S.C. §112, second paragraph. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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APPENDIX

Pending Claims 14, 15, 19 and 21-36 read as follows:

Claim 14. A method for preparing a vaccine against human immunodeficiency virus (HIV) comprising:

(a) introducing into a vector DNA or liposome a nucleic acid encoding an envelope glycoprotein of HIV, wherein said envelope glycoprotein comprises a deletion of the third variable loop (V3); and

(b) mixing said vector DNA or liposome with a suitable adjuvant.

Claim 15. The method of Claim 14, wherein said nucleic acid is introduced into antigen presenting cells (APCs) and said APCs are mixed with adjuvant.

Claim 19. A vaccine for inducing cellular immunity against HIV comprising:

(a) cells expressing on their surfaces an envelope glycoprotein of HIV, wherein said envelope glycoprotein comprises a deletion of the third variable loop (V3); and

(b) an adjuvant.

Claim 21. The method of Claim 14, wherein said deletion of the third variable loop (V3) comprises deletion of amino acids 297 to 329 in said variable loop.

Claim 22. The method of Claim 14, wherein said human immunodeficiency virus is human immunodeficiency virus 1 IIIB.

Claim 23. The vaccine of Claim 19, wherein said cells are antigen presenting cells.

Claim 24. The vaccine of Claim 19, wherein said deletion of the third variable loop (V3) comprises deletion of amino acids 297 to 329 in said variable loop.

Claim 25. The vaccine of Claim 19, wherein said human immunodeficiency virus is human immunodeficiency virus 1 IIIB.

Claim 26. A method for preparing a vaccine against human immunodeficiency virus (HIV) comprising:

(a) introducing into a vector DNA or liposome, a nucleic acid encoding an envelope glycoprotein of HIV 1-IIIB, wherein said envelope glycoprotein comprises a deletion of amino acids 297 to 329 in the third variable loop (V3); and

(b) mixing said vector DNA or liposome with a suitable adjuvant.

Claim 27. A vaccine for inducing cellular immunity against HIV comprising:

(a) antigen presenting cells expressing on their surfaces an envelope glycoprotein of HIV 1 IIIB, wherein said envelope glycoprotein comprises a deletion of amino acids 297 to 329 in the third variable loop (V3); and

(b) an adjuvant.

Claim 28. A method of preparing a composition for stimulating CTL activity against human immunodeficiency virus, comprising

(a) introducing into a vector DNA or liposome a nucleic acid encoding an envelope glycoprotein of HIV, wherein said envelope glycoprotein comprises a deletion of the third variable loop (V3); and

(b) mixing said vector DNA or liposome with a suitable adjuvant.

Claim 29. The method of Claim 28, wherein said nucleic acid is introduced into antigen presenting cells (APCs) and said APCs are mixed with adjuvant.

Claim 30. The method of Claim 28, wherein said deletion of the third variable loop (V3) comprises deletion of amino acids 297 to 329 in said variable loop.

Claim 31. The method of Claim 28, wherein said human immunodeficiency virus is human immunodeficiency virus 1 IIIB.

Claim 32. A method of stimulating a CTL response in a patient, comprising administering the composition prepared according to the method of Claim 28 to the patient in an amount sufficient to stimulate a CTL response.

Claim 33. A method of stimulating a CTL response in a patient, comprising administering the composition prepared according to the method of Claim 29 to the patient in an amount sufficient to stimulate a CTL response.

Claim 34. A method of stimulating a CTL response in a patient, comprising administering the composition prepared according to the method of Claim 30 to the patient in an amount sufficient to stimulate a CTL response.

Claim 35. A method of stimulating a CTL response in a patient, comprising administering the composition prepared according to the method of Claim 31 to the patient in an amount sufficient to stimulate a CTL response.

Claim 36. A method of stimulating a CTL response in a patient, comprising administering the composition prepared according to the method of Claim 32 to the patient in an amount sufficient to stimulate a CTL response.